| Notice of Allowability | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/063,583 | GODDARD ET AL. | |
| | Examiner | Art Unit | |
| | Jon M. Lockard | 1647 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--*

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *the Response filed 29 March 2006*.

2. ☒ The allowed claim(s) is/are *6-9 and 11-13 (renumbered as claims 1-7)*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
**THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS ( as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review ( PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   **Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).**

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

**Attachment(s)**

1. ☒ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date 3/29/06
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

*Continued Examination Under 37 CFR 1.114*

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 03/29/2006 has been entered.

## EXAMINER'S AMENDMENT

2. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with AnneMarie Kaiser on 27 July 2006.

The application has been amended as follows:

3. The title of the application has been amended as follows:

~~SECRETED AND TRANSMEMBRANE~~ PRO1335 POLYPEPTIDES ~~AND NUCLEIC ACIDS ENCODING THE SAME~~

4. Claims 10 and 14-17 have been cancelled without prejudice or disclaimer.

5. In claim 6, section (d) has been deleted.

6. In claim 6, the term "(e)" has been deleted and the term --(d)-- inserted therefor.

7. The following is an examiner's statement of reasons for allowance.

8. The claims of the instant invention are directed to an isolated polypeptide of SEQ ID NO:74. The specification provides several asserted utilities at page 93, including that the PRO1335 polypeptides of the present invention may be differentially expressed in a diseased tissue as compared to a normal tissue of the same tissue type.

9. Applicant states that the gene expression data in the specification, Example 18, shows that the mRNA associated with the PRO1335 polypeptide was more highly expressed in normal stomach, lung, rectum, and skin tissue compared to stomach, lung, rectum, and melanoma tumor tissue, respectively. Gene expression was analyzed using standard semi-quantitative PCR amplification reactions of cDNA libraries isolated from different human tumor and normal human tissue samples (See pg 140 of the Specification). Identification of the differential expression of the PRO1335 polypeptide-encoding gene in tumor tissue compared to the corresponding normal tissue renders the molecule useful and enabled as a diagnostic tool for the determination of the presence or absence of tumor.

10. Example 18 at page 140-144 of the instant specification demonstrates differential expression of PRO1335 cDNA using quantitative PCR amplification reactions. DNA62812-1594 was shown to be more highly expressed in normal stomach, lung, rectum, and skin tissue compared to stomach, lung, rectum, and melanoma tumor tissue, respectively, in this Example (See pg 142). Applicant states at page 9 of the response that Example 18 utilizes a more accurate and reliable method of assessing changes in mRNA levels, namely quantitative PCR analysis. Applicant relies on more than 140 references (see IDS filed 03/29/06), where expression levels

of mRNA, measured by quantitative PCR, were found to have a good correlation to the expressed protein levels.

11. It had been previously argued in the Office action mailed 28 December 2005 that mRNA levels were not predictive of protein levels, citing references by Haynes et al., Gygi et al., and Chen et al. However, these references were measuring and analyzing mRNA levels using microarrays, not using quantitative PCR analysis, and the art recognizes that the results obtained by microarray are not always the same as the results obtained using quantitative PCR (for example, see Oda et al. Virchows Arch. 430: 99-105, 1997, specifically page 104, column 1, paragraph 2). While the PTO found several references in which the protein expression levels did not correlate with mRNA levels measured by quantitative PCR (see Sugg et al., Clinical Endocrinology 49: 629-637, 1998; Toler et al., Am. J. Obstet. Gynecol. 194: e27-e31, 2006; Berner et al. Histopathol. 42:546-554, 2003; Brooks et al. Am. J. Physiol. Renal Physiol. 284: F218-F228, 2003), the majority of the references which were found, including those cited by Applicant, demonstrated a correlation between mRNA levels measured by quantitative PCR and protein expression levels.

12. Applicant asserts that the expression levels of protein correlate to mRNA (cDNA) levels when the cDNA is measured by quantitative PCR (i.e. rtPCR). Applicant has provided more than 140 references in support of this position. The prior art of record (Haynes et al., Gygi et al., Chen et al.), argued by the Examiner, is not specifically directed to message levels measured by rtPCR. Based on the totality of evidence of record, one of skill in the art would find it more

likely than not that an increase in message as measured by rtPCR would be predictive of an increase in protein expression levels, absent evidence to the contrary. Therefore, the data presented in Example 18, which demonstrates differential expression of nucleic acids encoding PRO1335, also supports a conclusion of differential expression of the PRO1335 polypeptide. Therefore, one of ordinary skill in the art would be able to use the PRO1335 polypeptide diagnostically for distinguishing stomach, lung, rectum, and melanoma tumor tissue from normal stomach, lung, rectum, and skin tissue, as asserted by Applicant.

13. Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

*Advisory Information*

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jon M. Lockard, Ph.D.** whose telephone number is **(571) 272-2717**. The examiner can normally be reached on Monday through Friday, 8:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Brenda Brumback**, can be reached on **(571) 272-0961**.

The fax number for the organization where this application or proceeding is assigned is **571-273-8300**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see **http://pair-direct.uspto.gov**. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

Jon M. Lockard, Ph.D.
July 27, 2006

BRENDA BRUMBACK
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600